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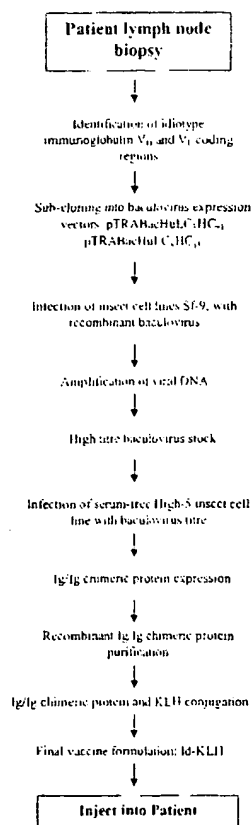
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[Continued on next page]

(54) Title: METHOD AND COMPOSITION FOR ALTERING A B CELL MEDIATED PATHOLOGY



(57) Abstract: The present invention provides a method for altering a B cell mediated pathology in a patient. This method comprises administering a composition comprising at least one and/or two chimeric proteins. Each chimeric protein comprises at least a portion of either the V_H or V_L region of a immunoglobulin molecule from particular B cells from a patient having a B cell mediated pathology, and an immunoglobulin constant region. The genes encoding V_H and/or V_L regions and the genes encoding immunoglobulin constant regions are isolated and inserted into an expression vector. The chimeric proteins are produced by introducing the expression vectors into insect cell lines. The chimeric proteins are purified using antibody affinity columns, and then chemically conjugated to an immunogenic carrier, keyhole-limpet hemocyanin (KLH). Since the conjugates comprise chimeric proteins made specifically from particular B cells from a patient having B cell mediated pathology, when it is administered to such a patient, with or without a cytokine, such as granulocyte-macrophage-CSF, or a chemokine, it can induce immune responses to alter such a B cell mediated pathology.

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patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/25204

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61P37/00 A61P35/00 A61K39/395 A61K39/385 C12N15/866
//C12N5/10,C07K16/00,G01N33/68,(A61K39/395,38:19)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, MEDLINE, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>TAO M-H ET AL: "IDIOTYPE/GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR FUSION PROTEIN AS A VACCINE FOR B-CELL LYMPHOMA" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 362, 22 April 1993 (1993-04-22), pages 755-758, XP002031411 ISSN: 0028-0836 figures 1,3</p> <p style="text-align: center;">--- -/--</p>	1-60

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

27 August 2002

Date of mailing of the international search report

13/09/2002

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/25204

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SELMAYR M ET AL: "B-CELL LYMPHOMA IDIOTYPES CHIMERIZED BY GENE TARGETING CAN INDUCE TUMOR IMMUNITY" CANCER GENE THERAPY, NORWALK, CT, US, vol. 7, no. 3, March 2000 (2000-03), pages 501-506, XP000972429 ISSN: 0929-1903 page 505; figure 2	1-60
X	BENVENUTI F ET AL: "Anti-idiotypic DNA vaccines for lymphoma immunotherapy require the presence of both variable region genes for tumor protection." GENE THERAPY, vol. 7, no. 7, April 2000 (2000-04), pages 605-611, XP001098032 ISSN: 0969-7128 abstract	1-60
X	CASPAR CLEMENS B ET AL: "Idiotypic vaccines for non-Hodgkin's lymphoma induce polyclonal immune responses that cover mutated tumor idiotypes: Comparison of different vaccine formulations." BLOOD, vol. 90, no. 9, 1997, pages 3699-3706, XP002211227 ISSN: 0006-4971 cited in the application page 3704; figure 1	1-60
A	US 4 816 249 A (LEVY RONALD ET AL) 28 March 1989 (1989-03-28) the whole document	1-60
A	US 5 972 334 A (DENNEY JR DAN W) 26 October 1999 (1999-10-26) the whole document	1-60
A	VEELKEN H ET AL: "RAPID EXPRESSION CLONING OF B CELL LYMPHOMA-DERIVED IMMUNOGLOBULIN GENES FOR ANTI-IDIOTYPIC VACCINATION AND FUNCTIONAL ANALYSES OF FAB-FRAGMENTS" BLOOD, W.B. SAUNDERS, PHILADELPHIA, VA, US, vol. 90, no. 10 SUPPL 1 PAR, 15 November 1997 (1997-11-15), page 515A XP000992835 ISSN: 0006-4971 the whole document	1-60

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/25204

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1-34 are directed to a method of treatment of the human body, the search has been carried out and based on the alleged effects of the composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/25204

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 4816249	A	28-03-1989	US 4661586 A	28-04-1987
US 5972334	A	26-10-1999	US 5776746 A	07-07-1998
			AU 716257 B2	24-02-2000
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			JP 2002509426 T	26-03-2002
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			WO 9741244 A1	06-11-1997
			ZA 9703701 A	04-02-1998